

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 18 April 2001 (18.04.01)	
International application No. PCT/EP99/05988	Applicant's or agent's file reference RP/PCT/99-3
International filing date (day/month/year) 12 August 1999 (12.08.99)	Priority date (day/month/year)
Applicant KERSTEN, Jean et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 07 March 2001 (07.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38
--	---

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 February 2001 (22.02.2001)

PCT

(10) International Publication Number
WO 01/12717 A1

(51) International Patent Classification⁷: C08L 25/10,
23/16, 23/04, 23/10

Amand (BE). LAMANT, Carole [FR/BE]; Parkstraat, 30,
B-1830 Machelen (BE). SNAPS, Jean-François [BE/BE];
Rue du Bossut, 40, B-1390 Nethen (BE).

(21) International Application Number: PCT/EP99/05988

(74) Agent: POWIS DE TENBOSSCHE, Roland; Cabinet
Bede S.A., Place de l'Alma, 3, B-1200 Brussels (BE).

(22) International Filing Date: 12 August 1999 (12.08.1999)

(25) Filing Language: English

(81) Designated States (*national*): AU, CA, JP, US.

(26) Publication Language: English

(84) Designated States (*regional*): European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE).

(71) Applicant (*for all designated States except US*): BAXTER
INTERNATIONAL INC. [US/US]; Building 22-E, One
Baxter Parkway, Deerfield, IL 60015 (US).

Published:

— With international search report.

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): KERSTEN, Jean
[BE/BE]; Chaussée de Tournai, 259, B-7931 Villers-Saint-

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



WO 01/12717 A1

(54) Title: THERMOPLASTIC COMPOSITION

(57) Abstract: Thermoplastic composition comprising a thermoplastic elastomer, a polyolefin resin, and possibly additive(s) and/or filler(s), characterized in that the thermoplastic elastomer is a mixture comprising a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which is at least partially cross-linked, the weight ratio not cross-linked thermoplastic SIS elastomer/thermoplastic elastomer at least partially cross-linked being comprised between 1:10 and 5:1, preferably between 1:6 and 2.5:1.

Thermoplastic composition

The present invention relates to a thermoplastic elastomer composition.

5 The prior art

US-RE 32,028 discloses a thermoplastic mixture of partially cross-linked rubber with a polyolefin. This thermoplastic mixture is not suitable for the manufacture of sealing means for pharmaceutical vial, due to a lack of thermal stability and/or to a
10 lack of irradiation stability, but essentially due to its easy fragmentation causing simple or multiple leaks after perforation with needles.

US 4,664,275 discloses sealing plug for pharmaceutical vial, said plug being made of a mixture containing partially cross-linked butyl rubber, a thermoplastic resin
15 and an inorganic powder having a particle size lower than 150µm. The butyl rubber has a high flexural modulus and has to contain a high amount of inorganic solid particles so as to provide a good resistance to the passage of gases. The presence of such a high proportion of solid particles in the mixture requires a vigorous mixing step so to ensure a substantially homogeneous distribution of the
20 particles in the mixture. Moreover, when puncturing such a plug with the needle of a syringe, a risk exists that solid particles are pulled away and fall into the pharmaceutical composition to be injected. Finally, the presence of such a high amount of solid particles restricts the possible re-use of the composition of the plugs, as said composition can only be re-used in the manufacture of articles in
25 which the presence of such solid particles is authorized, and as the re-homogenization of a thermoplastic mixture comprising particles of butyl rubber mixed with solid particles is complex and/or difficult to reach. In addition, a high level of solid particles increases the risks of fragmentation and associated leakage post puncturing.

Brief description of the invention

The present invention has for subject matter a thermoplastic composition which can be easily molded, injected or extruded without requiring the need of solid particles, a composition suitable for the manufacture of sealing plug ensuring a good gas sealing, an excellent closing of the passage due to the puncturing of the plug by means of a needle, and an excellent stability at a temperature of 121°C, as well as to γ -rays exposure. The composition according to the invention contains advantageously substantially thermoplastic components, where its manufacture, its use and its re-use is easy and not expensive.

The thermoplastic composition of the invention comprises a thermoplastic elastomer, a polyolefin resin, and possibly additive(s) and/or filler(s). The thermoplastic elastomer of the composition of the invention is a mixture comprising a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which is at least partially cross-linked, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer at least partially cross-linked being comprised between 1:10 and 5:1, preferably between 1:6 and 2.5:1.

Not cross-linked thermoplastic SIS elastomer means a block copolymer styrene/isoprene/styrene or a mixture of block copolymer styrene/isoprene and block copolymer styrene/isoprene/styrene, said copolymer having an elasticity, a resilience, a melting point or a softening point suitable for the manufacture of closing plugs, etc. However, long-term performance of not cross-linked thermoplastic SIS elastomer is not warranted due to poor creep properties. Preferably the not cross-linked thermoplastic SIS elastomer contains less than about 20% by weight bound styrene, most preferably less than 18% by weight bound styrene, for example between 10 and 16% by weight bound styrene. The molecular weight is advantageously comprised between 150,000 and 275,000, preferably between 200,000 and 240,000. Preferably said not cross-linked thermoplastic SIS has a broad molecular weight distribution. According to an

embodiment, the molecular weight of the thermoplastic SIS is comprised between 0.9 and 1.1 the average molecular weight of the thermoplastic SIS (the sum of the weight of the copolymer divided by the number of moles of copolymer).

- 5 The thermoplastic SIS elastomer has advantageously a very low halide salt content (due for example, to the use of halide salt, such as LiCl, for the copolymerisation process). For example the thermoplastic SIS contains less than 0.5% by weight halide salt with respect to the weight of not cross-linked thermoplastic SIS elastomer. Advantageously, the thermoplastic SIS contains less than 0.3% by
10 weight, preferably less than 0.2% by weight, most preferably less than 0.1% by weight halide salt with respect to the weight of not cross-linked thermoplastic SIS elastomer.

- Therefore, the thermoplastic composition of the invention is substantially free of
15 halide salt, for example contains less than 0.5% by weight halide salt, advantageously less than 0.3% by weight, preferably less than 0.2% by weight, most preferably less than 0.1% by weight halide salt.

- Thermoplastic elastomer which has been partially cross-linked means an elastomer
20 with a melting point or a softening point corresponding to the temperature of manufacture of the articles, the said elastomer being preferably cross-linked in presence of a polyolefin resin. Said partially cross-linked thermoplastic elastomer is for example EPM elastomer, EPDM elastomer, SIS elastomer, or a mixture thereof, and is mixed with a polyolefin resin, such as polyethylene, polypropylene,
25 copolymer of ethylene and propylene, or mixture thereof. By using an efficient amount of partially cross-linked thermoplastic elastomer (with respect to the amount of not cross-linked thermoplastic SIS elastomer) in the composition of the invention, the thermoplastic composition of the invention has improved long-term performance and other properties could be adjusted by varying the ratios.

30

Suitable polyethylenes which can be used in the composition of the invention are: ultra low density polyethylene (density of less than 0.91g/cm³), low density

polyethylene (density of less than 0.92 g/cm³), medium density polyethylene (0.926 to 0.94 g/cm³), high density polyethylene (more than 0.941 g/cm³), and mixture thereof.

- 5 Suitable polypropylenes are isotactic polypropylene, syndiotactic polypropylene, especially polypropylene with a high isotacticity, as well as copolymers with ethylene.

Copolymers of ethylene and propylene are for example amorphous copolymer
10 (random distribution of the ethylene and propylene units), crystalline copolymer.

The polyolefin has advantageously a melt flow index (MFI) lower than 20, preferably comprised between 0.3 and 20 for a polypropylene and between 0.5 and 10 for a polyethylene.

15

The thermoplastic elastomer is preferably only partly cross-linked. The cross-linking rate of the said elastomer can be determined by measuring the gel content of the thermoplastic elastomer in cyclohexane (measured after immersion of the elastomer in cyclohexane during 48 hours at 73°F (23°C)). The gel content
20 corresponds to the part of the elastomer which is insoluble in the cyclohexane. Said method is well-known in the art. A method for determining the cross-linking rate is disclosed in more details in ASTM D2765-90 (determination of gel content and swell ratio of cross-linked ethylene plastics).

- 25 The partial cross-linking of the elastomer is carried out by means of any known cross-linking agent. However, preferably, the cross-linking agent is a silane, for example a silane having hydrocarbon groups at least partly halogenated, a peroxide, organic peroxide, especially benzoyl peroxide and benzyl peroxide derivative. Other examples of possible peroxides are dicumyl peroxide, di-
30 butylperoxide, 2,5-dimethyl-2,5-di-(tert-butylperoxy)hexane, 2,5-dimethyl-2,5-di-(tert-butylperoxy)hexane-3, 1,3-bis(tert-butylperoxyisopropyl)benzene, 1,1-bis(tert-butylperoxy)-3,3,5-trimethylcyclohexane, n-butyl-4,4-bis(tert-

butylperoxy)valerate, p-chlorobenzoyl peroxide, 2,4-dichlorobenzoyl peroxide, tert-butylperoxybenzoate, tert-butylperoxyisopropyl carbonate, diacetyl peroxide, lauroyl peroxide, tert-butylcumyl peroxide, etc.

- 5 The partial cross-linking of the elastomer is preferably cross-linked in presence of a polyolefin resin, said cross-linking being advantageously carried out in a process in which the elastomer is partly cross-linked under conditions of high shear at a temperature above the melting point of the polyolefin component. The elastomer is thus simultaneously partly cross-linked and dispersed, for example as fine
- 10 particles, in the polyolefin. The partly cross-linking can be carried out in conventional mixing equipments, such as roll mills, bambury mixers, brabender mixers, continuous mixers, mixing extruders, etc. or in presence of water vapor fr the silanes.
- 15 Preferably, in the composition according to the invention, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer at least partially cross-linked + polyolefin resin is comprised between 1:5 and 1:1, the polyolefin resin being advantageously selected from the group consisting of polyethylene, polypropylene, and mixture of polyethylene and polypropylene. Especially, the
- 20 polyolefin resin and the at least partially cross-linked thermoplastic elastomer forms a premixture containing not cross-linked thermoplastic elastomer and partially cross-linked thermoplastic elastomer distributed in the polyolefin.

According to an advantageous embodiment, the at least partially cross-linked

25 thermoplastic elastomer has a cross-linking rate of more than 20%, preferably comprised between 25% and 75 %. Said cross-linking rate corresponds to a gel content measured by the ASTM method ASTM D2765-90.

According to a particular embodiment, the composition of the invention comprises

30 as thermoplastic elastomer and polyolefin resin, a mixture of polyolefin resin and SIS elastomer, the said mixture containing at least 40% by weight SIS elastomer

(preferably at most 70% by weight SIS elastomer), whereby the said mixture contains at least 20% by weight at least partially cross-linked SIS elastomer.

According to another embodiment, the composition of the invention comprises a
5 not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which
has been partly cross-linked in presence of a polyolefin, the weight ratio not cross-
linked thermoplastic SIS elastomer / thermoplastic elastomer which has been
partly cross-linked in presence of a polyolefin being comprised between 1:6 and
1:1, advantageously 1:4 and 7:10, preferably between 1:3 and 1:2.

10

According to another embodiment of the composition of the invention, it comprises
a polyolefin resin, a partially cross-linked thermoplastic elastomer and a not cross-
linked thermoplastic SIS elastomer, the weight content of partially cross-linked
15 elastomer with respect to the weight of polyolefin resin, partially cross-linked
thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being
comprised between 20 and 40%, while the weight content of not cross-linked
thermoplastic SIS elastomer with respect to the weight of polyolefin resin, partially
cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS
20 elastomer being comprised between 15 and 50%.

According to a detail of a possible embodiment, the composition comprises at least
20% by weight of a not cross-linked thermoplastic elastomer different from the not
cross-linked thermoplastic SIS elastomer. Preferably, the weight ratio not cross-
25 linked thermoplastic elastomer different from the thermoplastic SIS elastomer / not
cross-linked SIS thermoplastic elastomer is lower than 1:2, preferably lower than
1:10.

According to a detail of a composition according to the invention, the polyolefin
30 resin and the thermoplastic elastomer(s) is a substantially homogenous mixture of a
substantially homogenous premixture of a polyolefin and a partly cross-linked
thermoplastic elastomer, with a not cross-linked thermoplastic SIS elastomer. For

example, the premixture of polyolefin resin and partly cross-linked elastomer has the form of particles containing polyolefin and partly cross-linked elastomer, the said particles being mixed with particles of not cross-linked SIS thermoplastic elastomer.

5

Preferably, the composition of the invention comprises an amount of not cross-linked elastomer sufficient for ensuring a thermal stability at 121°C for at least 100 minutes, preferably for at least 180 minutes, and/or a γ irradiation stability of at least 20 KGray, preferably of at least 35 KGray.

10

In order to ensure a good control of the distribution of the components of the composition when manufacturing articles, the composition comprises advantageously at least a dye or a pigment. Said dye or pigment has preferably a melting point corresponding substantially to the melting point of the not cross
15 linked SIS elastomer or lower than the melting point of the not cross linked SIS elastomer.

20

The composition of the invention can possibly contain other additives or agents, for example if required for a specific use, such additives and agents are for example fillers, stabilizer, antioxidant, ultraviolet absorber, lubricant, foaming agent, antistatic agent, flame retardant, plasticizer, talc, calcium carbonate, carbon black, mica, glass fiber, carbon fiber, aramid resin, processing agent, silicone oil, etc.

25

In the composition of the invention, the not cross-linked thermoplastic SIS elastomer and the thermoplastic elastomer at least partially cross-linked have advantageously substantially the same density or specific gravity. For example, the density of the elastomer at least partially cross-linked is advantageously comprised between 0.95 and 1.05 x the density of the not cross linked thermoplastic SIS elastomer. The density of the not cross linked thermoplastic SIS elastomer and the
30 density of the thermoplastic elastomer at least partially cross linked are advantageously comprised between 0.93 and 0.98.

The invention relates also to specific articles, a part of which is made of a composition according to the invention. Such articles can be manufactured by known techniques, such as molding, injection, extrusion, etc.

5

Such an article is for example a sealing means for a container or vial (such as a plug or a stopper), at least a part of the said sealing means being made of a composition according to the invention.

- 10 Such a sealing means is for example intended for closing and sealing a pharmaceutical container or vial defining an inner volume, the said sealing means comprising a body, at least a part of which being made of a composition according to the invention. The said body can be associated to a layer contacting a surface of the vial or container when the sealing means closes the said container or vial.

15

- According to an advantageous embodiment, the sealing means is made at least partly of a composition according to the invention comprising a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof. When the said body is associated with a contact or surface layer or provided with such a layer, the said layer is at least partly made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

- 25 The composition according to the invention can be used for the manufacture of film, cloth, protecting cloth, such as finger protection, glove, etc. Preferably, the composition of the invention used comprises a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof. The film, cloth, etc has advantageously a multilayer structure, at least one layer being made of the composition according to the invention, while
- 30 at least another layer of the structure is essentially made of a polyolefin resin

selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

The film can be used for the manufacture of bags, injection bags, etc. For example, the film is folded so that parts of the film contact each other, parts of the film being
5 thereafter welded together.

Tube, cap, cap for protecting a needle of a syringe, etc. can also be made at least partly of a composition in accordance to the invention. Advantageously, the tube, cap, etc comprises at least a layer made of a composition according to the
10 invention.

According to a preferred embodiment, the tube comprises at least a first and a second layers made of a composition in accordance to the invention, the first layer having a not cross-linked SIS elastomer content lower than the not cross-linked
15 SIS elastomer of the second layer. For example, the said first layer contacts and covers the second layer, i.e. the said second layer being directed towards the inner side of the tube with respect to the first layer.

The invention relates also to a process for the manufacture of an article from a composition according to the invention. In said process, the said composition is
20 mixed at a temperature sufficient for the at least partial smelting of the not cross-linked SIS elastomer, and the said composition is thereafter transformed in the said articles.

Preferably, the said composition contains at least one dye or pigment having a melting point corresponding substantially to the melting point of the not cross-linked SIS elastomer. A control of the dye or pigment distribution in the transformed articles is carried out, and the mixing step is controlled so as to reach a substantially homogeneous distribution of the dye or pigment in a part of the
25 composition just before its transformation in the said article. This quick control step is advantageous in order to determine whether an at least substantially constant quality of the manufactured articles can be reached.
30

After the manufacture of the articles, for example by injection or extrusion or molding, the manufactured articles are advantageously cooled by means of water, for example in a water bath.

The manufactured articles, preferably after their passage through a water bath, are
5 advantageously sterilized at a temperature of 121°C during at least 100 minutes (for example during 180 minutes) and/or irradiated with a γ -irradiation of at least 20 KGray, for example 35 KGray.

Even if the composition of the invention ensures already excellent closing of the passage due to the puncturing of the plug by means of a needle, the composition
10 can possibly contain additives, such as an isoprene derivative such as squalene, phytol, etc. (derivatives listed in column 4 of US 5,904,967, the content of which is incorporated herein by reference).

The composition of the invention contains however preferably less than 20% by weight of such isoprene derivative(s), most preferably less than 10% by weight, for
15 example between 1 and 5% by weight.

Brief description of the drawings

Details and characteristics of the invention will appear from the following
20 description in which reference is done to the attached drawings. In these drawings,
- figure 1 is a cross section view of a stopper according to the invention ;
- figure 2 is a cross section of another stopper according to the invention ;
- figure 3 is a cross section of still another stopper according to the invention ;
- figure 4 is a cross section of a film according to the invention ;
25 - figure 5 is a partial perspective view of a bag according to the invention ; and
- figure 6 is a cross section view of a tube according to the invention.

Examples of compositions according to the inventionComposition 1

5

In a tumbler, 60 parts by weight of a mixture polypropylene(PP)/EPDM (partly cross linked linear EPDM) sold under the name SANTOPRENE® 281-45 (sold by Advanced Elastomer Systems, USA, technical characteristics : free flowing pellets; tensile strength 3 MPa –ASTM D 412; elongation ultimate 300% -ASTM D 412; density 0.97 g/cm³, hardness 45 Shore A –ASTM D 2240; processing temperature 175 to 230°C), 39 parts by weight of thermoplastic elastomer SIS (a linear block copolymer sold by Shell Chemicals under the name KRATON D1161NS ®, technical characteristics : in the form of powder or pellets; density 0.92 g/cm³ – ISO 2781; Melt Flow Rate at 200°C, 5kg : 12g/10minutes –ISO 1133 ; hardness, 30s : 30 Shore A – ISO 868; bound styrene content : about 15% by weight ; halide salt content : less than 0.2-0.3% by weight) and 1 part by weight of ultramarine blue (as master batch in polypropylene PP, melting point of about 160°C) have been mixed together.

20 The said mixture was used in a screw extruder so as to produce a continuous strip. The temperature of the extruder was about 180°C, while the screw was adapted so as to ensure a substantially homogeneous distribution of SIS elastomer in the Santoprene. The said homogeneous distribution is confirmed by the substantially uniform blue color of the strip during its extrusion.

25

Compositions 2 to 5

As for the composition 1, strips have been prepared by using SANTOPRENE – SIS mixture, the composition of which is given in the following table.

30

Composition	2	3	4	5	6	7
SANTOPRENE % by weight	50	80	75	60	65	70
SIS % by weight	50	20	24	40	35	29
Ultramarine blue as master batch in PP % by weight			1			1

Compositions 8 to 16

5

Strips have been prepared as for composition 1, except that SARLINK 3150N ® (a PP/radial cross linked EPDM sold by DSM, The Netherlands, technical features : specific gravity 0.94 g/cm³, Tensile strength 4.3 MPa – ISO 37; hardness, 5 seconds: 58°Shore A; Ultimate elongation 655%, melt temperature 185°C-220°C) has been used instead of SANTOPRENE 281. Details of the compositions are given in the following table.

10

composition	8	9	10	11	12	13	14	15	16
SARLINK % by weight	50	75	65	60	75	69	50	80	70
SIS % by weight	50	25	35	39	24	30	49	20	30
Ultramarine blue as master batch in PP % by weight				1	1	1	1		

Compositions 17 to 24

Strips have been prepared as for composition 1, except that a mixture of SARLINK
 5 3150N ® and SANTOPRENE 281 was used. Details of the compositions are given
 in the following table.

Composition	17	18	19	20	21	22	23	24
SANTOPRENE % by weight	40	35	30	50	10	25	14	50
SARLINK % by weight	40	30	35	10	50	25	50	14
SIS	20	34	34	40	40	49	35	35
Ultramarine blue as master batch in PP % by weight		1	1			1	1	1

10

Compositions 25 to 33

In a mixer, a polyolefin has been mixed with SIS elastomer at 180°C. After
 obtaining a substantially homogeneous mixture, benzoyl peroxide has been added
 15 to the mixture as cross-linking agent in a quantity corresponding to about 5% of the
 weight of the SIS elastomer and the partial cross linking was carried out at 180°C
 under shearing in the extruder screw. About 80 % of the SIS was not cross-linked.
 Possibly not cross-linked SIS elastomer was thereafter added.

20 The following table gives the composition of the thermoplastic elastomers
 manufactured.

The said manufactured elastomer strips were submitted to a sterilizing treatment with water vapor (121°C) during 180 minutes or left in open air for one week.

Compositions 43 to 58

5

These compositions have been prepared by adding to 100 parts by weight of one composition 1 to 16, y parts by weight of squalene. The following table gives the amount of squalene added.

Composition	100 parts by weight of composition n°	Y parts by weight of squalene
43	1	10
44	2	5
45	3	3
46	4	3
47	5	5
48	6	4
49	7	5
50	8	8
51	9	2
52	10	5
53	11	1
54	12	1
55	13	5
56	14	4
57	15	5
58	16	5

10

Examples of embodiments

Example of stoppers

15

Stopper n°1

The stopper of figure 1 is intended to close the opening of a neck of a pharmaceutical vial 100 (shown in dash line). Said stopper has a body 1 made of a composition according to the invention, the said body being provided on its face 10

20

directed towards the vial, with a layer 2 suitable to be in contact with the pharmaceuticals, and/or easy to clean and/or having other properties. Said layer is for example made of a polyolefin containing possibly additive(s), such as elastomers.

5

The polyolefin used in the layer is advantageously a polyethylene, a polypropylene, a copolymer of ethylene and propylene, or a mixture thereof. Preferably the polyolefin of the layer corresponds to the polyolefin or at least to one of the polyolefin used in the thermoplastic elastomer composition of the body 1. This is
10 advantageous for ensuring a good adhesion of the layer 2 on the body 1, and for re-using the composition of the stopper for the manufacture of new stoppers.

The stopper was sterilized with water vapor at 121°C during 180 minutes.

15 The sterilized stopper was used for closing and sealing a pharmaceutical vial containing a liquid. No release of particles from the stopper towards the liquid contained in the vial was observed. A injection needle of a syringe (diameter of the needle : respectively 0.8, 1.2 and 2.1 mm) was pushed through the stopper into the vial so as to pump liquid into the syringe (by means of the movement of the
20 plunger). After removal of the needle, the passage in the stopper due to the puncture of the needle was closed, and no liquid from the vial could flow through said passage. The test was repeated up to 10 times to challenge the closure with success.

25

The stopper can be manufactured by co-injecting a thermoplastic elastomer composition of the invention and a polyolefin in a mold.

The stopper of the invention was suitable for closing the passage created by a
30 needle, even when no lateral compression force was exerted on the stopper.

Stopper n°2

The stopper of figure 2 is similar to the stopper of figure 1, except that the stopper
5 has a sandwich structure, i.e. the thermoplastic elastomer composition of the
invention 20 is located between a first polyolefin layer 21 (compatible with the
liquid contained in the pharmaceutical vial, such as a polyethylene or a
polypropylene) and a second polyolefin layer 22 (such as a polyethylene or a
propylene.

10

Stopper n°3

The stopper of figure 3 is a multilayered stopper. Said stopper comprises an outer
layer 30 made in a material easy to clean (such as a polypropylene), a layer 31
15 made of a thermoplastic composition according to the invention, a layer 32 for
increasing the adherence of other layers on the layer 31, a layer 33 ensuring a
sealing or a permanent sealing of the neck of the container (for example a glue
layer, a hot melt layer, or any other material suitable to form a permanent bound or
a substantially permanent bound between the stopper and the neck, for example
20 after a heating, a radiation, etc.), and a layer 34 made of a material compatible with
the liquid of the container (for example polyethylene, polypropylene, ...).

Example of film

25 The elastomeric composition of the invention can be used for the manufacture of
films or support or plates, such as mono layer film or multi layer film. Figure 4
shows in cross section the structure of a multi layer film, said film having a central
portion 50 made of the composition according to the invention, and two outer
layers 51,52, preferably made of a polyolefin, such as polyethylene, polypropylene,
30 copolymer of ethylene and propylene. The total thickness of the film is for
example 50 µm to 10 mm, especially between 100 µm and 2 mm. The film can be
produced by co extrusion and can be subjected to a stretching (mono axial or

biaxial). The film can be used for the manufacture of stoppers, plugs, etc by thermoforming.

The film can also be used for the preparation of bags. The film is folded so that parts of the film contact each other. Thereafter, by means of a welding machine, a welding 53 between parts of the inner film 51 is formed along the edge of the bag.

The film can also be used for the manufacture of gloves, protecting fingers, strips to be placed on the skin of a patient where an injection has to be made.

10

Example of tube

The composition of the invention can be used for the manufacture of tube 60. Such a tube is advantageously a multi layer tube, which can be manufactured by co extrusion.

15

The tube has for example an inner compatible layer 61, for example a layer containing a few SIS elastomer, for example a polyolefin layer containing less than 10% SIS, a central layer 62 made of a composition according to the invention, and an outer polyolefin layer 63 containing no or a few SIS for giving a good abrasion resistance. The central layer 62 acts as a layer against leaks, even when the tube is punctured for example by means of a needle of syringe. Such a tube can be used for the manufacture of artificial veins, injection tube, for example a tube extending between a bag or baxter and a patient, whereby a pharmaceutical can be injected in the tube without creating a leakage, so that said pharmaceutical is injected through the injection site of the bag or baxter.

20
25

CLAIMS

- 5 1. Thermoplastic composition comprising a thermoplastic elastomer, a polyolefin resin, and possibly additive(s) and/or filler(s), characterized in that the thermoplastic elastomer is a mixture comprising a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which is at least partially cross-linked, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic
10 elastomer at least partially cross-linked being comprised between 1:10 and 5:1, preferably between 1:6 and 2.5:1.
2. The composition of claim 1, characterized in that the at least partially cross-linked thermoplastic elastomer is a thermoplastic elastomer at least partially cross-
15 linked in presence of a polyolefin resin.
3. The composition of claim 1 or 2, characterized in that the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer at least partially cross-linked + polyolefin is comprised between 1:5 and 1:1.
20
4. The composition of claim 1, characterized in that the polyolefin resin is selected in the group consisting of polyethylene, polypropylene, and mixture of polyethylene and polypropylene.
- 25 5. The composition of claim 1, characterized in that the polyolefin resin and the at least partially cross-linked thermoplastic elastomer forms a premixture containing not cross-linked thermoplastic elastomer and partially cross-linked thermoplastic elastomer.
- 30 6. The composition of claim 1, characterized in that the at least partially cross-linked thermoplastic elastomer has a cross-linking rate of more than 20%, preferably comprised between 25% and 75 %.

7. The composition of claim 1, characterized in that it comprises as thermoplastic elastomer and polyolefin resin, a mixture of polyolefin resin and SIS elastomer, the said mixture containing at least 40% by weight SIS elastomer, whereby the said
5 mixture contains at least 20% by weight at least partially cross-linked SIS elastomer.

8. The composition of claim 1, characterized in that it comprises a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which has been partly
10 cross-linked in presence of a polyolefin, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer which has been partly cross-linked in presence of a polyolefin being comprised between 1:6 and 1:1, advantageously 1:4 and 7:10, preferably between 1:3 and 1:2.

15 9. The composition of claim 1, characterized in that it comprises a polyolefin resin, a partially cross-linked thermoplastic elastomer and a not cross-linked thermoplastic SIS elastomer, the weight content of partially cross-linked elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised
20 between 20 and 40%, while the weight content of not cross-linked thermoplastic SIS elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised between 15 and 50%.

25 10. The composition of claim 1, characterized in that it comprises at least 20% by weight of a not cross-linked thermoplastic elastomer different from the not cross-linked thermoplastic SIS elastomer.

11. The composition of claim 10, characterized in that the weight ratio not cross-
30 linked thermoplastic elastomer different from the thermoplastic SIS elastomer / not cross-linked SIS thermoplastic elastomer is lower than 1:2, preferably lower than 1:10.

12. The composition of claim 1, characterized in that the polyolefin resin and the thermoplastic elastomer(s) is a substantially homogenous mixture of a substantially homogenous premixture of a polyolefin and a partly cross-linked thermoplastic elastomer, with a not cross-linked thermoplastic SIS elastomer.

13. The composition of claim 1, characterized in that a silane is used for the partial cross-linking of the thermoplastic elastomer.

14. The composition of claim 1, characterized in that it comprises an amount of not cross-linked elastomer sufficient for ensuring a thermal stability at 121°C of at least 100 minutes and/or a γ irradiation stability of at least 20 KGray.

15. The composition of claim 1, characterized in that it comprises at least a dye or a pigment.

16. The composition of claim 1, characterized in that it comprises less than 0.5% by weight halide salt.

17. The composition of claim 16, characterized in that it comprises less than 0.3% by weight, preferably less than 0.2% by weight, most preferably less than 0.1% by weight halide salt.

18. Sealing means for a container or vial, at least a part of the said sealing means being made of a composition according to one of the preceding claims.

19. The sealing means according to claim 18, for sealing a pharmaceutical container or vial defining an inner volume, the said sealing means comprising a body, at least a part of which being made of a composition according to one of the claims 1 to 17, the said body being associated to a layer contacting a surface of the vial or container when the sealing means closes the said container or vial.

20. The sealing means according to claim 19, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the said layer is at least partly made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

21. Film, cloth, protecting cloth comprising at least a layer made of a composition in accordance to one of the claims 1 to 17.

22. The film, cloth or protecting cloth of claim 21, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the film, cloth or protecting cloth comprises at least one layer essentially made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

23. Tube or cap, cap for protecting a needle of a syringe, the said tube or cap comprising at least one layer made of a composition in accordance to one of the claims 1 to 17.

24. Tube in accordance to claim 23, characterized in that it comprises at least a first and a second layers made of a composition in accordance to one of the claims 1 to 17, a first layer having a not cross-linked SIS elastomer content lower than the not cross-linked SIS elastomer of the second layer.

25. Bag made of a film according to claim 21 or 22.

26. Process for the manufacture of an article from a composition according to one of the claims 1 to 17, in which the said composition is mixed at a temperature

sufficient for the at least partial smelting of the not cross-linked SIS elastomer, and in which the said composition is thereafter transformed in the said articles.

27. The process of claim 26, in which the said composition contains at least one
5 dye or pigment having a melting point corresponding substantially to the melting
point of the not cross-linked SIS elastomer, in which a control of the dye or
pigment distribution in the transformed articles is carried out, and in which the
mixing step is controlled so as to reach a substantially homogeneous distribution of
the dye or pigment in a part of the composition just before its transformation in the
10 said article.

28. The process of claim 27, in which the said article is sterilized at a temperature
of 121°C during at least 100 minutes and /or irradiated with a γ -irradiation of at
least 20 KGray.

15

1/2

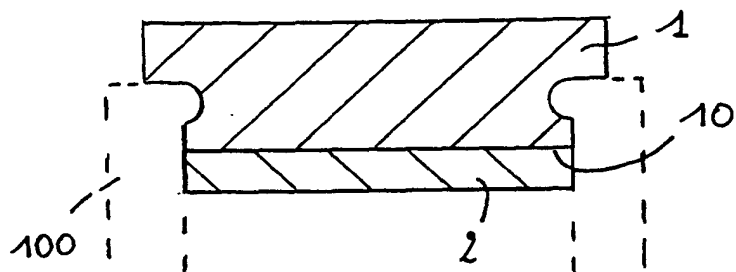


FIG 1

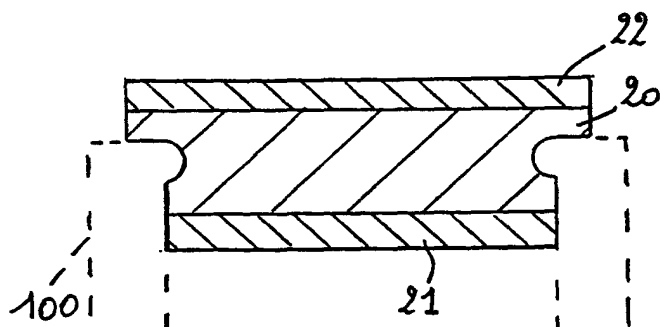


FIG 2

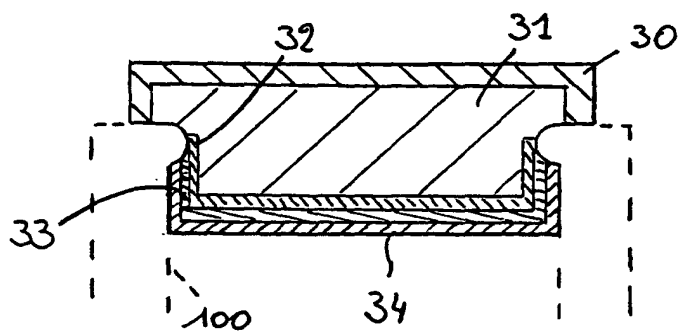


FIG 3

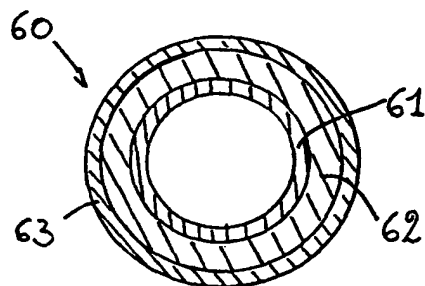
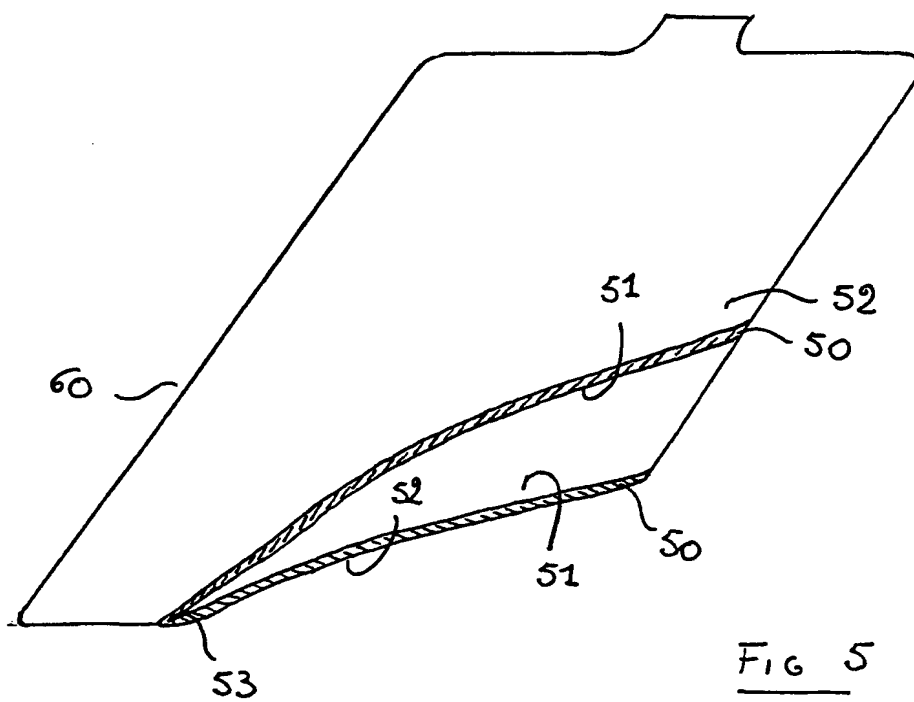
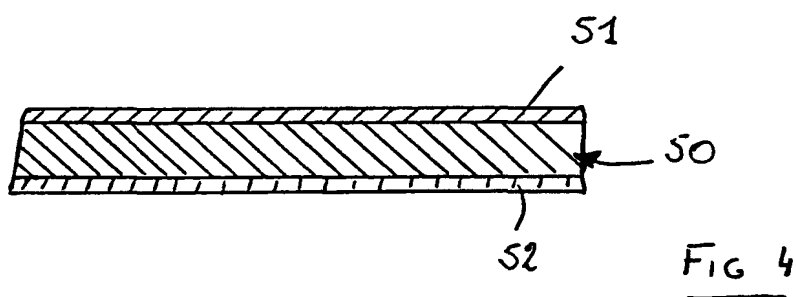


FIG 6



INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/05988

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C08L25/10 C08L23/16 C08L23/04 C08L23/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 87 05310 A (TOA NENRYO KOGYO KK) 11 September 1987 (1987-09-11) abstract; claim 1 page 1, line 3,4 page 4, line 1-10 page 5, line 26-40 page 6, line 18,25-40 page 7, line 1-40 page 8, line 5 page 9, line 20,21 ---	1-17
A	WO 96 18678 A (EXXON CHEMICAL PATENTS INC) 20 June 1996 (1996-06-20) abstract; claims 1-8 page 1, line 5-15 page 6, line 20-35 page 7, line 25-35 --- -/--	1-25



Further documents are listed in the continuation of box C:



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 April 2000

Date of mailing of the international search report

08/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31.651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bergmans, K

INTERNATIONAL SEARCH REPORT

Inte. .onal Application No

PCT/EP 99/05988

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 4 607 074 A (HAZELTON DONALD R ET AL)</p> <p>19 August 1986 (1986-08-19)</p> <p>abstract; claims 1-49</p> <p>column 1, line 5-15</p> <p>column 3, line 19-21,60,61</p> <p>column 5, line 5-25</p> <p>column 8, line 33</p> <p>-----</p>	1-28

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/05988

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8705310 A	11-09-1987	JP 62201951 A	05-09-1987
		AU 604691 B	03-01-1991
		AU 7163287 A	28-09-1987
		CA 1271286 A	03-07-1990
		EP 0258419 A	09-03-1988
		US 4871796 A	03-10-1989
WO 9618678 A	20-06-1996	US 5635262 A	03-06-1997
		AT 177460 T	15-03-1999
		CA 2208232 A	20-06-1996
		DE 69508278 D	15-04-1999
		DE 69508278 T	30-09-1999
		EP 0797622 A	01-10-1997
US 4607074 A	19-08-1986	AU 594926 B	22-03-1990
		AU 4483185 A	16-01-1986
		CA 1258934 A	29-08-1989
		DE 3587228 A	06-05-1993
		DE 3587228 T	21-10-1993
		EP 0171926 A	19-02-1986
		ES 545031 D	01-06-1987
		ES 8706181 A	16-08-1987
		JP 1944120 C	23-06-1995
		JP 6074357 B	21-09-1994
		JP 61026643 A	05-02-1986
		US 4960830 A	02-10-1990
		US 5086121 A	04-02-1992
		US 4845145 A	04-07-1989

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference RP/PCT/99-3	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.</small>	
International application No. PCT/EP 99/ 05988	International filing date (day/month/year) 12/08/1999	(Earliest) Priority Date (day/month/year)

Applicant

BAXTER INTERNATIONAL INC. et. al.

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/05988

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C08L25/10 C08L23/16 C08L23/04 C08L23/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 87 05310 A (TOA NENRYO KOGYO KK) 11 September 1987 (1987-09-11) abstract; claim 1 page 1, line 3,4 page 4, line 1-10 page 5, line 26-40 page 6, line 18,25-40 page 7, line 1-40 page 8, line 5 page 9, line 20,21 ---	1-17
A	WO 96 18678 A (EXXON CHEMICAL PATENTS INC) 20 June 1996 (1996-06-20) abstract; claims 1-8 page 1, line 5-15 page 6, line 20-35 page 7, line 25-35 ---	1-25
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

19 April 2000

Date of mailing of the international search report

08/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bergmans, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/05988

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 607 074 A (HAZELTON DONALD R ET AL) 19 August 1986 (1986-08-19) abstract; claims 1-49 column 1, line 5-15 column 3, line 19-21, 60, 61 column 5, line 5-25 column 8, line 33 -----	1-28

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No



PCT/EP 99/05988

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8705310 A	11-09-1987	JP 62201951 A	05-09-1987
		AU 604691 B	03-01-1991
		AU 7163287 A	28-09-1987
		CA 1271286 A	03-07-1990
		EP 0258419 A	09-03-1988
		US 4871796 A	03-10-1989
WO 9618678 A	20-06-1996	US 5635262 A	03-06-1997
		AT 177460 T	15-03-1999
		CA 2208232 A	20-06-1996
		DE 69508278 D	15-04-1999
		DE 69508278 T	30-09-1999
		EP 0797622 A	01-10-1997
US 4607074 A	19-08-1986	AU 594926 B	22-03-1990
		AU 4483185 A	16-01-1986
		CA 1258934 A	29-08-1989
		DE 3587228 A	06-05-1993
		DE 3587228 T	21-10-1993
		EP 0171926 A	19-02-1986
		ES 545031 D	01-06-1987
		ES 8706181 A	16-08-1987
		JP 1944120 C	23-06-1995
		JP 6074357 B	21-09-1994
		JP 61026643 A	05-02-1986
		US 4960830 A	02-10-1990
		US 5086121 A	04-02-1992
		US 4845145 A	04-07-1989

REC'D 31 DEC 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RP/PCT/99-3		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/05988	International filing date (day/month/year) 12/08/1999	Priority date (day/month/year) 12/08/1999	
International Patent Classification (IPC) or national classification and IPC C08L25/10			
Applicant BAXTER INTERNATIONAL INC. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 6 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application			
Date of submission of the demand 07/03/2001		Date of completion of this report 27.12.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Barker, S Telephone No. +49 89 2399 8526 	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/05988

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-17	as originally filed			
18	as received on	21/11/2001	with letter of	20/11/2001

Claims, No.:

1-29	as received on	21/11/2001	with letter of	20/11/2001
------	----------------	------------	----------------	------------

Drawings, sheets:

1/2,2/2	as originally filed
---------	---------------------

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/05988

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,4,8-12,14-16,19-26,28,29
	No:	Claims	1,3,5-7,13,17,18,27
Inventive step (IS)	Yes:	Claims	2,8,9,11,12,14,15,19-26,28,29
	No:	Claims	4,10,16
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re. part V

- 1).
 - a) Having regard to the disclosure in the document WO 87/05310 (D1) which is cited in the International Search Report (ISR), the subject matter of claims 1,3,5-7,13, and 27 is considered to lack novelty. Accordingly, the subject matter of these claims does not fulfil the criterion of Art.33(2) PCT.
 - b) Reference is made to those parts of D1 mentioned in the ISR as well as page 3 and the passage at pages 9 to 11 under the heading, "Method of Manufacturing the Composition". There is disclosed a thermoplastic elastomer composition which necessarily contains a polyolefin resin (F) (see pages 5-6) and a partially crosslinked thermoplastic elastomer of component (G) (see page 6). To the composition formed from components (A) to (F) there is added component (G) which is partially crosslinked (vulcanised) by the peroxide (H). To that intermediate product is then added, by melt blending, the unvulcanised elastomer (I) which is chosen from a list which includes unvulcanised SIS elastomer in amounts which have a large degree of overlap with the present claim 1. The styrene content of the styrenic rubbers disclosed is in the range of 5-70 wt.%. The lower limit of 5 wt.% is generally applicable to all styrenic rubbers disclosed, including the SIS block copolymer, therefore the added feature, in present claim 1, of a styrene content of less than 20 wt.% provides no distinction over claim 1. Articles are formed from the final, uniform compositional product. The absence of examples in D1 using SIS block copolymer as the styrenic rubber does not negate the presence of novelty-destroying disclosure in the general description.
 - c) The subject matter of present claims 7,17,18 may well be intrinsic in the products of D1.
 - d) It would appear that a composition of claim 6 would be indistinguishable from the compositions of D1.
 - e) The subject matter of claims 2,8,9,11,12,14,15,19-26,28 and 29 is considered to be new over D1 and does not appear to be suggested by the disclosure of D1. (Arts.33(2) and (3) PCT)
- 2). The subject matter of claims 4, 10 and 16 is considered to lack an inventive step over the disclosure in D1 as it lies within its teachings and has not been shown provide any surprising effect. The applicant has argued that D1 does not disclose or suggest the improved sealing plugs referred to in the present

description. That observation is not disputed but it is noted that the claims in question are far broader and relate to compositions per se, and that the present examples do not appear to comprise appropriate comparative examples based on the closest prior art (D1) on which the criticality, with respect to an objective technical problem, of the narrower ranges could be recognised. Accordingly, these claims do not fulfil the criterion of Art.33(3) PCT.

- 3). a) The subject matter of claims 1-29 is recognised to be new and to involve an inventive step over the documents WO 96/18678 A (D2) and US 4607074 A (D3) for the following reasons.
- b) The compositions of D2 appear to neither disclose nor suggest the presence of a thermoplastic elastomer which is at least partially crosslinked.
- c) The compositions of D3 appear to neither disclose nor suggest the presence of a SIS copolymer or a thermoplastic elastomer which is at least partially crosslinked.
- 4). The subject matter of the claims 1-29 is considered to be capable of industrial application. (Art.33(4) PCT)

Re. part VIII

- 5). The description should be adapted to agree with the scope of the claims (Art.6 PCT).

biaxial). The film can be used for the manufacture of stoppers, plugs, etc by thermoforming.

The film can also be used for the preparation of bags. The film is folded so that parts of the film contact each other. Thereafter, by means of a welding machine, a welding 53 between parts of the inner film 51 is formed along the edge of the bag.

The film can also be used for the manufacture of gloves, protecting fingers, strips to be placed on the skin of a patient where an injection has to be made.

10

Example of tube

The composition of the invention can be used for the manufacture of tube 60. Such a tube is advantageously a multi layer tube, which can be manufactured by co
15 extrusion.

The tube has for example an inner compatible layer 61, for example a layer containing a few SIS elastomer, for example a polyolefin layer containing less than 10% SIS, a central layer 62 made of a composition according to the invention, and
20 an outer polyolefin layer 63 containing no or a few SIS for giving a good abrasion resistance. The central layer 62 acts as a layer against leaks, even when the tube is punctured for example by means of a needle of syringe. Such a tube can be used for the manufacture of artificial veins, injection tube, for example a tube extending between a bag or baxter and a patient, whereby a pharmaceutical can be injected in
25 the tube without creating a leakage, so that said pharmaceutical is injected through the injection site of the bag or baxter. ②

such as bags sold under the trademark

Amended claims

1. Thermoplastic composition comprising a thermoplastic elastomer mixture containing at least a styrenic elastomer, a polyolefin resin, and possibly additives(s) and/or filler(s), in which the thermoplastic elastomer mixture comprises :
 - a not cross-linked thermoplastic SIS elastomer contains less than 20% by weight bound styrene, advantageously less than 18% by weight bound styrene, preferably from 10 to 16% by weight bound styrene, and
 - a thermoplastic elastomer which is at least partially cross-linked, the weight ratio not cross-linked thermoplastic SIS elastomer/thermoplastic elastomer at least partially cross-linked being comprised between 1 :10 and 5 :1, preferably between 1 :6 and 2.5 :1.
2. The composition of claim 1, characterized in that the not crosslinked SIS elastomer has a molecular weight comprised between 150,000 and 275,000, advantageously between 200,000 and 240,000.
3. ~~2.~~ The composition of claim 1, ^{or 2} characterized in that the at least partially cross-linked thermoplastic elastomer is a thermoplastic elastomer at least partially cross-linked in presence of a polyolefin resin.
4. ~~3.~~ The composition of claim 1 or 2, ^{or 3} characterized in that the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer at least partially cross-linked + polyolefin is comprised between 1:5 and 1:1.
5. ~~4.~~ The composition of claim 1, characterized in that the polyolefin resin is selected in the group consisting of polyethylene, polypropylene, and mixture of polyethylene and polypropylene.
6. ~~5.~~ The composition of claim 1, characterized in that the polyolefin resin and the at least partially cross-linked thermoplastic elastomer forms a premixture containing not cross-linked thermoplastic elastomer and partially cross-linked thermoplastic elastomer.
7. ~~6.~~ The composition of claim 1, characterized in that the at least partially cross-linked thermoplastic elastomer has a cross-linking rate of more than 20%, preferably comprised between 25% and 75 %.

AMENDED SHEET

87. The composition of claim 1, characterized in that it comprises as thermoplastic elastomer and polyolefin resin, a mixture of polyolefin resin and SIS elastomer, the said mixture containing at least 40% by weight SIS elastomer, whereby the said mixture contains at least 20% by weight at least partially cross-linked SIS elastomer.

98. The composition of claim 1, characterized in that it comprises a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which has been partly cross-linked in presence of a polyolefin, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer which has been partly cross-linked in presence of a polyolefin being comprised between 1:6 and 1:1, advantageously 1:4 and 7:10, preferably between 1:3 and 1:2.

109. The composition of claim 1, characterized in that it comprises a polyolefin resin, a partially cross-linked thermoplastic elastomer and a not cross-linked thermoplastic SIS elastomer, the weight content of partially cross-linked elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised between 20 and 40%, while the weight content of not cross-linked thermoplastic SIS elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised between 15 and 50%.

110. The composition of claim 1, characterized in that it comprises at least 20% by weight of a not cross-linked thermoplastic elastomer different from the not cross-linked thermoplastic SIS elastomer.

111. The composition of claim 10, characterized in that the weight ratio not cross-linked thermoplastic elastomer different from the thermoplastic SIS elastomer / not cross-linked SIS thermoplastic elastomer is lower than 1:2, preferably lower than 1:10.

AMENDED SHEET

¹³~~12~~. The composition of claim 1, characterized in that the polyolefin resin and the thermoplastic elastomer(s) is a substantially homogenous mixture of a substantially homogenous premixture of a polyolefin and a partly cross-linked thermoplastic elastomer, with a not cross-linked thermoplastic SIS elastomer.

¹⁴~~13~~. The composition of claim 1, characterized in that a silane is used for the partial cross-linking of the thermoplastic elastomer.

¹⁵~~14~~. The composition of claim 1, characterized in that it comprises an amount of not cross-linked elastomer sufficient for ensuring a thermal stability at 121°C of at least 100 minutes and/or a γ irradiation stability of at least 20 KGray.

¹⁶~~15~~. The composition of claim 1, characterized in that it comprises at least a dye or a pigment.

¹⁷~~16~~. The composition of claim 1, characterized in that it comprises less than 0.5% by weight halide salt.

¹⁸~~17~~. The composition of claim ¹⁷~~16~~, characterized in that it comprises less than 0.3% by weight, preferably less than 0.2% by weight, most preferably less than 0.1% by weight halide salt.

¹⁹~~18~~. Sealing means for a container or vial, at least a part of the said sealing means being made of a composition according to one of the preceding claims.

²⁰~~19~~. The sealing means according to claim ¹⁹~~18~~, for sealing a pharmaceutical container or vial defining an inner volume, the said sealing means comprising a body, at least a part of which being made of a composition according to one of the claims 1 to ¹⁸~~17~~, the said body being associated to a layer contacting a surface of the vial or container when the sealing means closes the said container or vial.

²¹
20. The sealing means according to claim ²⁰~~19~~, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the said layer is at least partly made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

²²
21. Film, cloth, protecting cloth comprising at least a layer made of a composition in accordance to one of the claims 1 to ²²~~17~~.

²³
22. The film, cloth or protecting cloth of claim ²³~~21~~, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the film, cloth or protecting cloth comprises at least one layer essentially made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

²⁴
23. Tube or cap, cap for protecting a needle of a syringe, the said tube or cap comprising at least one layer made of a composition in accordance to one of the claims 1 to ²⁴~~17~~.

²⁵
24. Tube in accordance to claim ²⁵~~23~~, characterized in that it comprises at least a first and a second layers made of a composition in accordance to one of the claims 1 to ²⁶~~18~~~~17~~, a first layer having a not cross-linked SIS elastomer content lower than the not cross-linked SIS elastomer of the second layer.

²⁶
25. Bag made of a film according to claim ²⁷~~21~~ or ²⁸~~22~~.

²⁷
26. Process for the manufacture of an article from a composition according to one of the claims 1 to ²⁹~~17~~, in which the said composition is mixed at a temperature

sufficient for the at least partial smelting of the not cross-linked SIS elastomer, and in which the said composition is thereafter ^{shaped} transformed in the said articles.

- ²⁸
27. The process of claim ²⁷26, in which the said composition contains at least one
5 dye or pigment having a melting point corresponding substantially to the melting
point of the not cross-linked SIS elastomer, in which a control of the dye or
pigment distribution in the transformed articles is carried out, and in which the
mixing step is controlled so as to reach a substantially homogeneous distribution of
the dye or pigment in a part of the composition just before ^{the shaping of} its transformation in the
10 said article.

- ²⁸
²³28. The process of claim ²⁸27, in which the said article is sterilized at a temperature
of 121°C during at least 100 minutes and /or irradiated with a γ -irradiation of at
least 20 KGray.

15

biaxial). The film can be used for the manufacture of stoppers, plugs, etc by thermoforming.

5 The film can also be used for the preparation of bags. The film is folded so that parts of the film contact each other. Thereafter, by means of a welding machine, a welding 53 between parts of the inner film 51 is formed along the edge of the bag.

The film can also be used for the manufacture of gloves, protecting fingers, strips to be placed on the skin of a patient where an injection has to be made.

10

Example of tube

The composition of the invention can be used for the manufacture of tube 60. Such a tube is advantageously a multi layer tube, which can be manufactured by co
15 extrusion.

The tube has for example an inner compatible layer 61, for example a layer containing a few SIS elastomer, for example a polyolefin layer containing less than 10% SIS, a central layer 62 made of a composition according to the invention, and
20 an outer polyolefin layer 63 containing no or a few SIS for giving a good abrasion resistance. The central layer 62 acts as a layer against leaks, even when the tube is punctured for example by means of a needle of syringe. Such a tube can be used for the manufacture of artificial veins, injection tube, for example a tube extending between a bag or baxter and a patient, whereby a pharmaceutical can be injected in
25 the tube without creating a leakage, so that said pharmaceutical is injected through the injection site of the bag or baxter.

CLAIMS

- 5 1. Thermoplastic composition comprising a thermoplastic elastomer, a polyolefin resin, and possibly additive(s) and/or filler(s), characterized in that the thermoplastic elastomer is a mixture comprising a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which is at least partially cross-linked, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic
10 elastomer at least partially cross-linked being comprised between 1:10 and 5:1, preferably between 1:6 and 2.5:1.
2. The composition of claim 1, characterized in that the at least partially cross-linked thermoplastic elastomer is a thermoplastic elastomer at least partially cross-
15 linked in presence of a polyolefin resin.
3. The composition of claim 1 or 2, characterized in that the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer at least partially cross-linked + polyolefin is comprised between 1:5 and 1:1.
20
4. The composition of claim 1, characterized in that the polyolefin resin is selected in the group consisting of polyethylene, polypropylene, and mixture of polyethylene and polypropylene.
- 25 5. The composition of claim 1, characterized in that the polyolefin resin and the at least partially cross-linked thermoplastic elastomer forms a premixture containing not cross-linked thermoplastic elastomer and partially cross-linked thermoplastic elastomer.
- 30 6. The composition of claim 1, characterized in that the at least partially cross-linked thermoplastic elastomer has a cross-linking rate of more than 20%, preferably comprised between 25% and 75 %.

7. The composition of claim 1, characterized in that it comprises as thermoplastic elastomer and polyolefin resin, a mixture of polyolefin resin and SIS elastomer, the said mixture containing at least 40% by weight SIS elastomer, whereby the said
5 mixture contains at least 20% by weight at least partially cross-linked SIS elastomer.

8. The composition of claim 1, characterized in that it comprises a not cross-linked thermoplastic SIS elastomer and a thermoplastic elastomer which has been partly
10 cross-linked in presence of a polyolefin, the weight ratio not cross-linked thermoplastic SIS elastomer / thermoplastic elastomer which has been partly cross-linked in presence of a polyolefin being comprised between 1:6 and 1:1, advantageously 1:4 and 7:10, preferably between 1:3 and 1:2.

15 9. The composition of claim 1, characterized in that it comprises a polyolefin resin, a partially cross-linked thermoplastic elastomer and a not cross-linked thermoplastic SIS elastomer, the weight content of partially cross-linked elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised
20 between 20 and 40%, while the weight content of not cross-linked thermoplastic SIS elastomer with respect to the weight of polyolefin resin, partially cross-linked thermoplastic elastomer and not cross-linked thermoplastic SIS elastomer being comprised between 15 and 50%.

25 10. The composition of claim 1, characterized in that it comprises at least 20% by weight of a not cross-linked thermoplastic elastomer different from the not cross-linked thermoplastic SIS elastomer.

11. The composition of claim 10, characterized in that the weight ratio not cross-
30 linked thermoplastic elastomer different from the thermoplastic SIS elastomer / not cross-linked SIS thermoplastic elastomer is lower than 1:2, preferably lower than 1:10.

12. The composition of claim 1, characterized in that the polyolefin resin and the thermoplastic elastomer(s) is a substantially homogenous mixture of a substantially homogenous premixture of a polyolefin and a partly cross-linked thermoplastic elastomer, with a not cross-linked thermoplastic SIS elastomer.

13. The composition of claim 1, characterized in that a silane is used for the partial cross-linking of the thermoplastic elastomer.

14. The composition of claim 1, characterized in that it comprises an amount of not cross-linked elastomer sufficient for ensuring a thermal stability at 121°C of at least 100 minutes and/or a γ irradiation stability of at least 20 KGray.

15. The composition of claim 1, characterized in that it comprises at least a dye or a pigment.

16. The composition of claim 1, characterized in that it comprises less than 0.5% by weight halide salt.

17. The composition of claim 16, characterized in that it comprises less than 0.3% by weight, preferably less than 0.2% by weight, most preferably less than 0.1% by weight halide salt.

18. Sealing means for a container or vial, at least a part of the said sealing means being made of a composition according to one of the preceding claims.

19. The sealing means according to claim 18, for sealing a pharmaceutical container or vial defining an inner volume, the said sealing means comprising a body, at least a part of which being made of a composition according to one of the claims 1 to 17, the said body being associated to a layer contacting a surface of the vial or container when the sealing means closes the said container or vial.

20. The sealing means according to claim 19, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the said layer is at least partly made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

21. Film, cloth, protecting cloth comprising at least a layer made of a composition in accordance to one of the claims 1 to 17.

22. The film, cloth or protecting cloth of claim 21, characterized in that the polyolefin resin of the composition in accordance to one of the claims 1 to 17 is selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof, while the film, cloth or protecting cloth comprises at least one layer essentially made of a polyolefin resin selected from the group consisting of polyethylene, polypropylene, copolymer of ethylene-propylene and mixture thereof.

23. Tube or cap, cap for protecting a needle of a syringe, the said tube or cap comprising at least one layer made of a composition in accordance to one of the claims 1 to 17.

24. Tube in accordance to claim 23, characterized in that it comprises at least a first and a second layers made of a composition in accordance to one of the claims 1 to 17, a first layer having a not cross-linked SIS elastomer content lower than the not cross-linked SIS elastomer of the second layer.

25. Bag made of a film according to claim 21 or 22.

26. Process for the manufacture of an article from a composition according to one of the claims 1 to 17, in which the said composition is mixed at a temperature

sufficient for the at least partial smelting of the not cross-linked SIS elastomer, and in which the said composition is thereafter transformed in the said articles.

27. The process of claim 26, in which the said composition contains at least one
5 dye or pigment having a melting point corresponding substantially to the melting
point of the not cross-linked SIS elastomer, in which a control of the dye or
pigment distribution in the transformed articles is carried out, and in which the
mixing step is controlled so as to reach a substantially homogeneous distribution of
the dye or pigment in a part of the composition just before its transformation in the
10 said article.

28. The process of claim 27, in which the said article is sterilized at a temperature
of 121°C during at least 100 minutes and /or irradiated with a γ -irradiation of at
least 20 KGray.